

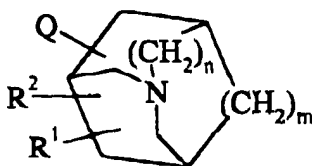
AMENDMENTS

Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

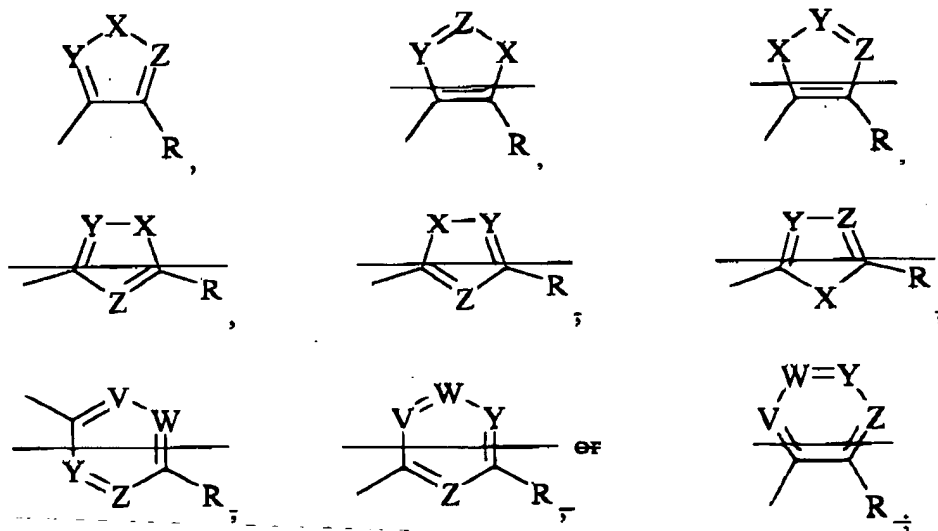
Listing of claims:

1. (currently amended) A pharmaceutical composition comprising at least one M4 selective muscarinic agonist selected from the azacyclic ring system having the formula I



I

including ~~and~~ geometrical isomers, enantiomers, diastereomers, racemates, acid addition salts, salts thereof with a pharmaceutically acceptable acid, and prodrugs thereof, wherein Q is



X is ~~CH₂, NH, O or S~~;

V, W, Y and Z ~~independently~~ are CH or N;

n and m independently are 0, ~~1, 2, 3 or 4~~;

R^1 and R^2 are at any position on the azacyclic ring, including the point of attachment of the heterocycle Q, and independently are hydrogen, -OH, halogen, -NH₂, carboxy, straight or branched C₁₋₁₀-alkyl, C₁₋₁₀-alkenyl, or C₁₋₁₀-alkynyl, straight or branched C₁₋₁₀-alkoxy, or straight or branched C₁₋₁₀-alkyl substituted with -OH, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

R^1 and R^2 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, or C₁₋₁₀-alkylthio;

R is hydrogen, halogen, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

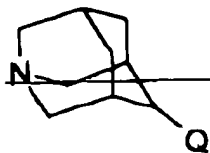
R is phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C₁₋₁₅-alkyl, C₁₋₁₀-alkoxy, or C₁₋₁₀-alkylthio; or

R is a 5 or 6 membered saturated, partly saturated or aromatic heterocyclic ring containing one to three heteroatoms; and

R^3 and R^4 independently are straight, branched, or cyclic C₁₋₁₅-alkyl, C₂₋₁₅-alkenyl, C₂₋₁₅-alkynyl, or combinations thereof, or R^3 and R^4 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl groups, each of which are unsubstituted or substituted with H, halogen, -CN, C₁₋₁₅-alkyl, C₁₋₁₀-alkoxy, C₁₋₁₀-alkylthio, or aryl; or

R^3 and R^4 independently are 5 or 6 membered saturated, partly saturated or aromatic heterocyclic rings containing one to three heteroatoms; and further comprising one or more additional analgesics.

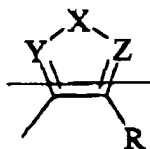
2. (currently amended) The composition according to claim 1 wherein in formula I of the M4 selective muscarinic agonist n and m both are 1 and the azacyclic ring system has the structural formula:



H

wherein

Q is:



X is S,

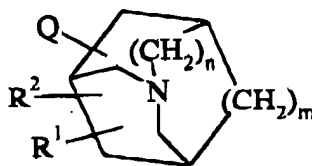
Y and Z are N, and

R is OR³ or SR³.

3. (original) The composition according to claim 2 wherein R³ of the M4 selective muscarinic agonist is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃ or -CH₂CH(CH₃)₂.
4. (original) The composition according to claim 1 wherein the M4 selective muscarinic agonist is selected from the group consisting of
- 3-(5-Aza-2-chlorotricyclo[3.3.1.1<3,7>]dec-2-yl)-4-chloro-1,2,5-thiadiazole;
 - 3-(5-Azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-chloro-1,2,5-thiadiazole;
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-methoxy-1,2,5-thiadiazole;
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-ethoxy-1,2,5-thiadiazole;
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-propoxy-1,2,5-thiadiazole;
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-butoxy-1,2,5-thiadiazole;
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-(cyclopropylmethoxy)-1,2,5-thiadiazole; and
 - 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-(2-methyl-propoxy)-1,2,5-thiadiazole;
 - 4-[4-(propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane hydrochloride
 - 4-[4-(methylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane
 - 4-[4-(ethylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane

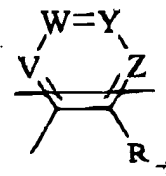
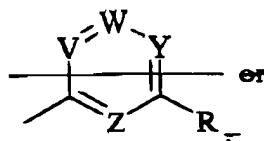
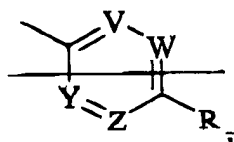
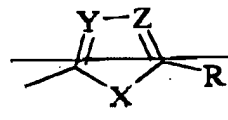
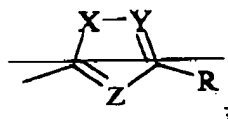
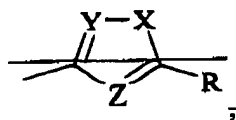
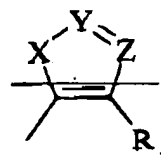
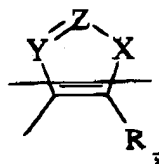
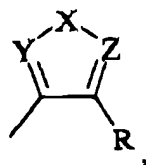
- l) 4-[4-(butylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane
m) 4-[4-(2-methyl-propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane
n) 4-[4-(cyclopropylmethylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane.

5. (original) The composition according to claim 4 wherein the M4 selective muscarinic agonist is 4-s-[4-(propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane hydrochloride.
6. (original) The composition according to claim 1 further comprising a pharmaceutically acceptable carrier.
7. (original) The composition according to claim 1 wherein the additional analgesic is selected from the group of opioid analgesics, nonsteroidal anti-inflammatory drugs and other analgesics.
8. (original) The composition according to claim 7 wherein the additional analgesic is an opioid analgesic.
9. (original) The composition according to claim 8 wherein the opioid analgesic is selected from the group of morphine and codeine.
10. (original) The composition according to claim 7 wherein the additional analgesic is a non-steroidal anti-inflammatory drug.
11. (original) The composition according to claim 10 wherein the non-steroidal anti-inflammatory drug is selected from the group of acetaminophen, ibuprofen, celecoxib and rofecoxib.
12. (original) The composition according to claim 7 wherein the additional analgesic is selected from the group of nicotinic agonists, NMDA antagonists, epileptics and alpha adrenoceptor agonists.
13. (withdrawn) A method of inducing analgesia, the method comprising co-administration of at least one M4 selective muscarinic agonist selected from the azacyclic ring system having the formula I



I

including and geometrical isomers, enantiomers, diastereomers, racemates, acid addition salts, salts thereof with a pharmaceutically acceptable acid, and prodrugs thereof, wherein Q is



X is ~~CH₂, NH, O or S~~;

V, W, Y and Z independently are ~~CH or N~~;

n and m independently are ~~0, 1, 2, 3 or 4~~;

R¹ and R² are at any position on the azacyclic ring, including the point of attachment of the heterocycle Q, and independently are hydrogen, -OH, halogen, -NH₂, carboxy, straight or branched C₁₋₁₀-alkyl, C₁₋₁₀-alkenyl, or C₁₋₁₀-alkynyl, straight or branched C₁₋₁₀-alkoxy, or straight or branched C₁₋₁₀-alkyl substituted with -OH, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

R^1 and R^2 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C_{1-10} -alkyl, C_{1-10} -alkoxy, or C_{1-10} -alkylthio;

R is hydrogen, halogen, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

R is phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C_{1-15} -alkyl, C_{1-10} -alkoxy, or C_{1-10} -alkylthio; or

R is a 5 or 6 membered saturated, partly saturated or aromatic heterocyclic ring containing one to three heteroatoms; and

R^3 and R^4 independently are straight, branched, or cyclic C_{1-15} -alkyl, C_{2-15} -alkenyl, C_{2-15} -alkynyl, or combinations thereof, or R^3 and R^4 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl groups, each of which are unsubstituted or substituted with H, halogen, -CN, C_{1-15} -alkyl, C_{1-10} -alkoxy, C_{1-10} -alkylthio, or aryl; or

R^3 and R^4 independently are 5 or 6 membered saturated, partly saturated or aromatic heterocyclic rings containing one to three heteroatoms; with one or more additional analgesics.

14. (withdrawn) A method of inducing analgesia according to claim 13, the method comprising administering an analgesia-inducing amount of a composition according to claim 1 to a mammal in need thereof.
15. (canceled) A composition according to claim 1 for use as a medicament.
16. (canceled) A composition according to claim 1 for use as an analgesic.
17. (canceled) Use of the composition according to claim 1 for the manufacture of a medicament for treatment of analgesia.